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Variant: NM_001754.5(RUNX1):c.1271C>A (p.Ser424Ter)

Version: 1.1

CA410147557

2757091 (ClinVar)

Gene: RUNX1 (HGNC:861)
Condition: hereditary thrombocytopenia and hematologic cancer predisposition syndrome (MONDO:0011071)
Inheritance Mode: Autosomal dominant inheritance
UUID: d494eb32-e830-4058-8d88-61a282649f6a
Approved on: Mon, 05 Oct 2026 00:00:00 +0000
Published on: Mon, 05 Oct 2026 00:00:00 +0000

HGVS expressions

NM_001754.5(RUNX1):c.1271C>A (p.Ser424Ter)
NM_001754.5:c.1271C>A
NC_000021.9:g.34792307G>T
CM000683.2:g.34792307G>T
NC_000021.8:g.36164604G>T
CM000683.1:g.36164604G>T
NC_000021.7:g.35086474G>T
NG_011402.2:g.1197405C>A
ENST00000675419.1:c.1271C>A
ENST00000300305.7:c.1271C>A
ENST00000344691.8:c.1190C>A
ENST00000399240.5:c.998C>A
ENST00000437180.5:c.1271C>A
ENST00000482318.5:c.*861C>A
NM_001001890.2:c.1190C>A
NM_001754.4:c.1271C>A
NM_001001890.3:c.1190C>A

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PVS1_Strong PM5_Supporting

Not Met criteria codes 23

BA1 PP1 PP2 PP3 PP4 PM6 PM1 PM3 PM4 BS1 BS4 BS3 BS2 PS1 PS2 PS3 PS4 BP5 BP7 BP4 BP3 BP1 BP2

Evidence Links 0

Expert Panel

Myeloid Malignancy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Myeloid Malignancy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RUNX1 Version 3.1*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Myeloid Malignancy VCEP

NM_001754.5(RUNX1):c.1271C>A (p.Ser424Ter) is a nonsense variant which is not predicted to undergo NMD (PVS1_Strong). This variant is downstream of c.98 (PM5_Supporting) and is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting). In summary, this variant meets criteria to be classified as likely pathogenic. ACMG/AMP criteria applied, as specified by the ClinGen Myeloid Malignancy Variant Curation Expert Panel for RUNX1: PVS1_Strong, PM5_Supporting, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is completely absent from all population databases with at least 20x coverage for RUNX1 (PM2_Supporting), gnomAD v3.
PVS1_Strong	✔	This variant is not predicted to undergo NMD, but the truncated/altered region is critical for protein function (c.917-c.1440 as per VCEP specifications) (PVS1_Strong).
PM5_Supporting	✔	This variant is a nonsense variant that is downstream of c.98 (PM5_Supporting).

Not Met criteria codes

BA1	✖	This variant does not have a MAF ≥ 0.0015 (0.15%) in any general continental population dataset.
PP1	✖	Segregation data for this variant has not been reported in literature.
PP2	✖	not applicable
PP3	✖	Since this is not a missense variant, it has no REVEL score. SpliceAI score is 0.0. However is it highly conserved PhyloP 9.0.
PP4	✖	not applicable
PM6	✖	De novo data for this variant has not been reported in literature.
PM1	✖	This variant is not a missense variant.
PM3	✖	not applicable
PM4	✖	This variant is not an in-frame deletion/insertion.
BS1	✖	This variant does not have a MAF between 0.00015 (0.015%) and 0.0015 (0.15%) in any general continental dataset.
BS4	✖	Segregation data for this variant has not been reported in literature.

BS3	ℹ	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
BS2		✖	not applicable
PS1	ℹ	✖	This is not a missense variant.
PS2		✖	De novo data for this variant has not been reported in literature.
PS3	ℹ	✖	In vitro or in vivo functional data has not been reported for this variant in the literature.
PS4	ℹ	✖	Proband data for this variant has not been reported in literature.
BP5		✖	not applicable
BP7	ℹ	✖	This variant is not a synonymous or intronic variant.
BP4	ℹ	✖	Since this is not a missense variant, it has no REVEL score. SpliceAI score is 0.0. However is it highly conserved PhyloP 9.0.
BP3		✖	not applicable
BP1		✖	not applicable
BP2	ℹ	✖	This variant has not been observed in trans with a pathogenic variant for a fully penetrant dominant gene/disorder or observed in cis with a pathogenic variant in any inheritance pattern.

Curation History

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